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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,405	09/29/2005	Jay A Berzofsky	015280-481100US	4476

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EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	

MAIL DATE	DELIVERY MODE
04/15/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,405	BERZOFSKY ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7,17-19,22-31 and 33-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 7, 17-19, 22-31, and 33-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Office Action

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the communication filed 08 January, 2009. Claims 1-4, 7, 17-19, 22-31, and 33-41 are pending in the instant application.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

The previous rejection of claims 5 and 6 under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement, is moot in view of applicants' response.

Claims 3 and 4 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed toward a pharmaceutical, or medicament, composition comprising an immunostimulatory HIV-1 CTL peptide. The term "pharmaceutical" or "medicament" has an art-recognized meaning and refers to a composition that is utilized to treat a

particular malady. Moreover, the disclosure clearly stipulates that the claimed polypeptides may be employed in an HIV vaccine to treat or prevent HIV infection. No other disclosed "pharmaceutical" uses are provided.

The legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth. *Enzo Biochem, Inc.*, 52 U.S.P.Q.2d 1129 (C.A.F.C. 1999). *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

1) The state-of-the-art as it pertains to HIV vaccine development is characterized by a lack of success. Several factors have contributed to the failure of vaccine development including the quasispecies nature of HIV infection which leads to rapid immune escape, a lack of understanding of the correlates of protection, a lack of suitable animal models with which to test vaccine efficacy, and the down-regulation of cellular molecules required for antigen presentation and processing (Leslie *et al.*, 2004; Johnson *et al.*, 1992; Feinberg

et al., 2002; Letvin *et al.*, 2003; Yang *et al.*, 2003; and Connick *et al.*, 2007).

2) The disclosure fails to provide any working embodiments. Considering the unpredictability of the art, some type of working embodiment would be require to enable the claimed invention.

3) The disclosure fails to provide any guidance pertaining to the correlates of human protection. The claimed polypeptide comprises a modified CTL epitope. However, it is not readily manifest from reviewing the specification if the claimed polypeptides of interest can generate an antiviral response of sufficient specificity, magnitude and duration to inhibit viral replication to any meaningful extant.

When all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation to practice the claimed invention.

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 39 and 40 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Two separate requirements are set forth under this statute: (1) the claims must set forth the subject matter that applicants regard as their invention; and

(2) the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant. Both claims reference immunostimulating polypeptides with X_1 and X_3 groups, but not corresponding X_2. Thus, the metes and bounds of the patent protection desired cannot be ascertained.

35 U.S.C. § 103(a)

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 7, 17, 30, 33-36, and 39-41 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Herrer *et al.* (1996) in view of Sarobe *et al.* (1998). The claims are directed toward immunostimulatory polypeptides comprising the amino acid sequences X_1LYQYMDDV, VLYQYMDDV, X_1X_2LYQYMDDVX_3, and YLYQYMDDV. These peptides correspond to amino acid residues 179-187 of the human immunodeficiency virus type 1 (HIV-1) reverse transcriptase (RT). Herrer *et al.* (1996) identify an HLA-A2-restricted HIV-1 CTL epitope from an asymptomatic long-term nonprogressor (LTNP) comprising the following sequence: IV**I**YQYMDD**L** (bold-faced residues differ from the claimed polypeptides). This region corresponds to amino acids 179-187 of

the HIV-1 RT. This teaching does not disclose polypeptides comprising the amino acid sequence X_1**L**YQYMDD**V**. However, Sarobe *et al*. (1998) performed epitope optimization studies and demonstrated that substitution of the canonical anchor residues at positions 2 and 9 leads to a loss of CTL recognition. For HLA-A2 CTL epitopes these anchor residues are **L2** and **V9**. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the HIV-1 CTL epitope of Herrer *et al*. (1996), to include the canonical L2 and V9 anchor residues, since Sarobe *et al*. (1998) demonstrate that these anchor residues are required for optimal MCH class I binding.

Claims 18, 19, 24, 28, 29, and 37 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Herrer *et al*. (1996) in view of Sarobe *et al*. (1998), as applied *supra* to claims 1, 2, 7, 17, 30, 33-36, and 39-41, and further in view of Bolognesi *et al*. (2000, U.S. Patent No. 6,133,418). The claims further stipulate that the peptide of interest is modified at the amino or carboxyl terminus. Bolognesi and colleagues provide HIV-1 fusion inhibitory polypeptides with acetylated N-termini and carboxylated C-termini. The modification of these polypeptides facilitates their conjugation to other macromolecular carriers, as well as, imaging and diagnostic reagents. Various methods of preparing said polypeptides are also provided. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the polypeptides of Herrer *et al*. (1996) and Sarobe *et al*. (1998), as disclosed by Bolognesi *et al*. (2000), since this would facilitate the

conjugation of these polypeptides to macromolecular carriers, imaging reagents, and diagnostic reagents.

Claims 22, 23, and 25-27 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Herrer *et al.* (1996) in view of Sarobe *et al.* (1998), as applied *supra* to claims 1, 2, 7, 17, 30, 33-36, and 39-41, and further in view of Berzofsky *et al.* (1999). The claims are directed toward various conjugates comprising the CTL epitope of interest. Berzofsky and associates disclose the preparation of cluster, or fusion, polypeptides comprising CTL, humoral, and T-helper HIV epitopes fused to one another. The authors teach that said cluster peptides induce strong broad spectrum anti-HIV immune responses. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the polypeptides of Herrer *et al.* (1996) and Sarobe *et al.* (1998), to include additional T-helper epitopes and fusion epitopes, as provided by Berzofsky *et al.* (1999), since this would facilitate the development of strong anti-HIV CTL and neutralizing antibody responses.

Claims 31 and 38 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Herrer *et al.* (1996) in view of Sarobe *et al.* (1998), as applied *supra* to claims 1, 2, 7, 17, 30, 33-36, and 39-41, and further in view of Berzofsky *et al.* (2001). The claims are directed toward peptide-pulsed dendritic cells (DCs) comprising the CTL epitope of interest. Berzofsky and associates discuss the utilization of peptide-pulsed dendritic cells for the development of strong anti-HIV immune responses. Therefore, it would have been *prima facie* obvious to one of

ordinary skill in the art at the time of the invention to employ peptide-pulsed dendritic cells, as discussed by Berzofsky *et al.* (2001), comprising the polypeptides of Herrer *et al.* (1996) and Sarobe *et al.* (1998), since this would facilitate the development of strong anti-HIV CTL and neutralizing antibody responses.

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Larry R. Helms, can be reached at (571) 272-0832. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through

Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

/Jeffrey S. Parkin/

Jeffrey S. Parkin, Ph.D.
Primary Examiner, Art Unit 1648

13 April, 2009